RESEARCH ARTICLE

Economic Burden of Home Antimicrobial Therapy: OPAT Versus Oral Therapy

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ABSTRACT

BACKGROUND: There is increasing evidence that outpatient parenteral antimicrobial therapy (OPAT) is overused for children and that outcomes with oral therapy are equivalent. Our objective was to compare economic burden between OPAT and oral therapy, accounting for direct and indirect costs and caregiver quality of life (QoL).

METHODS: We conducted a prospective cohort study of caregivers for children after hospitalization who were treated with prolonged antimicrobial therapy. We collected data about missed work and school and time spent administering therapy. Caregivers completed the Pediatric Quality of Life Inventory to assess QoL. Clinical information included length of stay, treatment indication, and type of therapy (OPAT versus oral therapy). Direct medical costs were obtained by using a microcosting system and accounted for medication, supplies, and home-nursing visits. The primary cost outcome was the mean daily cost of therapy. Multivariable models were developed to adjust for potential confounders.

RESULTS: Two hundred and twelve caregivers completed surveys: 123 (58%) for oral therapy and 89 (42%) for OPAT. Caregivers administering OPAT reported more missed work, missed school for their children, time with daily medication administration (90 vs 6 minutes; $P < .01$) and lower QoL scores (77.8 vs 68.9) than caregivers administering oral therapy. The mean daily cost was $65 (95% confidence interval: $51–$78) for OPAT and $7 (95% confidence interval: $4–$9) for oral therapy. Relative differences in cost and QoL between groups did not change after model adjustment.

CONCLUSIONS: The overall burden of OPAT is substantially higher than that of oral therapy, including higher direct and indirect costs and greater impact on caregiver QoL. These findings strongly support efforts to use oral therapy in place of OPAT when clinically appropriate.

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Outpatient parenteral antimicrobial therapy (OPAT) is the administration of intravenous antimicrobial therapy in the home environment. OPAT is usually used to treat serious infections that require prolonged antimicrobial therapy after hospital discharge.[1] Favorable clinical outcomes have been demonstrated in multiple studies in which OPAT was compared with prolonged hospitalization.[1,2] Additionally, OPAT offers several potential advantages, including lower medical costs than continued hospitalization and earlier hospital discharge. Earlier return to the home environment allows patients and their caregivers to resume activities such as work and school and may enhance overall quality of life (QoL).[2,3]

However, recent studies reveal that OPAT is frequently overused in pediatrics, especially in instances in which a highly bioavailable oral antimicrobial may be substituted for intravenous therapy.[4,5] Additionally, a growing body of evidence reveals that oral antimicrobial therapy is likely to be equally effective in treating serious infections that have traditionally been treated with OPAT, including complicated pneumonia, intraabdominal infections, osteomyelitis, and endocarditis.[6–13]

Unnecessary OPAT administration exposes children and their caregivers to potentially complex medical, economic, and social challenges. In pediatrics, OPAT is usually administered by a caregiver using a peripherally inserted central catheter (PICC) placed during hospitalization. Catheter-related complications occur in 10% to 40% of patients receiving OPAT and are completely avoided with oral therapy.[4,5,14–18]

The direct medical costs of OPAT are substantial because of the relatively high costs of intravenous medications and the need for administrative equipment and home-nursing visits. The indirect costs of OPAT in pediatrics may also be substantial (including time spent administering medication). OPAT requires caregivers to administer drugs, often several times per day, flush the catheter, and sometimes perform dressing changes. Collectively, this requires a substantial amount of caregiver time and may result in missed work, missed leisure activities, altered child care arrangements, and decreased caregiver well-being. The child may forgo regular activities, such as playing sports, swimming, and bathing, and may have to miss school. The demands of OPAT may significantly decrease the family's QoL. From the perspective of the health care system, OPAT also demands significant time for care coordination by medical care providers, much of which may not be reimbursable.[19]

Existing economic evaluations of pediatric OPAT are limited by small sample sizes, and indirect costs or caregiver QoL has not been assessed in studies.[2,20] Additionally, although there has been substantial research in which clinical outcomes between oral antimicrobial therapy and OPAT are compared,[8–10,12] there are no economic evaluations in which these 2 treatment modalities are compared. Our objective for this study was to compare the economic burden, including direct and indirect costs, and caregiver QoL between OPAT and oral antimicrobial therapy for children with serious infections requiring prolonged home treatment.

METHODS

Human Subjects' Protection

This study was reviewed and approved by the institutional review boards of the study institution.

Study Design and Population

We conducted a prospective cohort study of patient caregivers designed to assess the economic and QoL burden of antimicrobial treatment in the home environment. Caregivers were eligible to participate if they identified themselves as a primary caregiver for a child who had been discharged from a 289-bed freestanding children's hospital to complete antimicrobial therapy at home. The hospital serves a large referral region encompassing parts of 5 states. Caregivers were approached during an initial follow-up visit at a university-based pediatric infectious diseases clinic after hospitalization. The clinic is staffed by pediatric infectious diseases physicians, a nurse practitioner, and clinical fellows. The study enrollment period was from September 2014 to June 2017.

Data Acquisition

Data were obtained from 2 sources: (1) a caregiver survey (see Supplemental Fig 3) and (2) medical record abstraction. A data collection instrument (English language only) was administered electronically to caregivers. The instrument was refined after pilot testing among a group of pediatric infectious diseases specialists and caregivers. Participants were assigned to either the OPAT or oral therapy category on the basis of the mode of therapy prescribed at the time of hospital discharge.

Caregiver Survey

After obtaining informed consent, the caregiver completed the survey during the clinic visit using a tablet device. The survey included questions about comfort with the process of antimicrobial administration (1 = very uncomfortable; 5 = very comfortable) and burden of administration (1 = not a burden; 3 = a minor burden; 5 = a major burden) for both caregiver and child by using a 5-point Likert scale. To measure components of costs from the caregiver perspective, caregivers reported direct costs as their out-of-pocket medical expenses and indirect costs as daily time in minutes spent administering antimicrobial agents, number of days of missed day care or school (for the patient) and work (for the caregiver[s]), and out-of-pocket travel and child care expenses. We measured caregiver QoL using the Family Impact Module of the Pediatric Quality of Life Inventory.[21] This validated 36-item survey is designed to assess QoL for caregivers of children with chronic conditions by addressing 8 domains: physical, social, emotional, cognitive, activity, communication, worry, and assessment of family functioning.[21] Respondents use a 5-point scale ranging from 0 (never a problem) to 4 (always a problem). The responses are aggregated and transformed to a 100-point scale, with higher numbers associated with better functioning.

Medical Record Abstraction

A trained study member (L.E.) reviewed medical records to collect demographic and

clinical information, including hospital length of stay, ICU admission, clinical indication for treatment, and antimicrobial agents prescribed after discharge, including dose, frequency, and duration. The direct medical costs associated with antimicrobial therapy consisted of 3 aggregated components: the daily medication cost (derived from the wholesale acquisition cost and accounting for route and dosage and multiplied by the duration in days), the cost of OPAT supplies for administration, and the cost of weekly nursing visits. The Intermountain Homecare pharmacy microcosting system, which reflects the perspective of the health care system,[22] was used to estimate costs of supplies and administration, accounting for the number of daily doses and duration (OPAT only) and for a once weekly nursing visit (OPAT only; $91). As a representative example, for 1 patient treated for 15 days with ceftriaxone, the aggregate cost is estimated as $16 for medication, $175 for supplies and administration, and $182 for 2 nursing visits for a total of $373. Charges were not measured.

Outcomes and Statistical Analysis

Outcomes were compared between those prescribed OPAT and those prescribed oral therapy at discharge. Descriptive statistics, including mean, median, and interquartile range, were calculated as appropriate. The direct medical costs for antimicrobial therapy for both the OPAT and oral therapy groups were standardized to an average daily cost by dividing the total aggregated cost for each group by the aggregated duration of therapy. A crude analysis included calculation of relative risk estimates and marginal means to estimate the effect of group assignment (OPAT versus oral therapy) on our primary outcomes, which included average daily direct medical cost and QoL score. To adjust for potential differences between the OPAT and oral therapy groups, we developed generalized multivariable models that were used to adjust for ICU admission, length of stay, treatment duration, age, race, and sex. To further minimize differences between subjects in the OPAT and oral therapy groups driven by diagnoses, we performed a subgroup analysis limiting our analysis sample to patients with osteomyelitis, complicated pneumonia, and intraabdominal infections. We selected these conditions because evidence reveals that patients have equivalent clinical outcomes when treated with OPAT or oral antimicrobial therapy.[6–10,12]

RESULTS

Demographics and Clinical Data

There were 485 potentially eligible subjects during the study period, of whom 222 were available for study coordinators to approach for participation. A total of 212 (95%) caregivers consented and completed the survey, including 89 (42%) caregivers of children receiving OPAT and 123 (58%) caregivers of children treated with oral antimicrobial therapy. Surveys were completed ~2 weeks after hospital discharge (Table 1). There were no differences in age, sex, or race of patients between the 2 groups (Table 1). Children receiving OPAT had longer hospital stays, were more likely to have been treated in the ICU, and had a longer duration of antimicrobial use after hospital discharge (Table 1). Patients with central nervous infections and endocarditis were more likely to be discharged with OPAT, whereas patients with osteomyelitis and pneumonia were more likely to be discharged with oral therapy (Table 1). The most commonly administered antimicrobial agents in the OPAT group were ceftriaxone (27 of 89; 30%), cefazolin (23 of 89; 26%), and ertapenem (9 of 89; 10.1%). The most common agents in the oral group were cephalexin (49 of 123; 40%), clindamycin (24 of 123; 20%), and amoxicillin (21 of 123; 17%).

Caregiver Comfort and Burden

Caregivers administering OPAT reported that they were significantly less comfortable with the treatment regimen at the time of hospital discharge compared with

TABLE 1 Demographic and Clinical Characteristics of Study Participants

Characteristic	Oral Antimicrobial Agents (n = 123)	OPAT (n = 89)	P
Age, y, mean ± SD	7.25 ± 4.92	8.38 ± 6.29	.160
Boys, *n* (%)	67 (54.5)	54 (60.67)	.368
Race, *n* (%)			.097
White	104 (84.6)	80 (89.9)	
Asian American	0 (0.0)	3 (3.37)	—
African American	5 (4.07)	0 (0)	
American Indian	2 (1.63)	1 (1.12)	
Native Hawaiian or Pacific Islander	9 (7.32)	3 (3.37)	
Multiracial	1 (0.81)	1 (1.12)	
Unknown	2 (1.63)	1 (1.12)	
Clinical indication, *n* (%)			
CNS infection	4 (3.25)	32 (36.0)	<.001
Endocarditis	0 (0.00)	5 (5.62)	.012
Osteomyelitis and/or septic arthritis	76 (61.8)	23 (25.9)	<.001
Pneumonia	23 (18.7)	2 (2.25)	<.001
Intraabdominal infection	5 (4.07)	5 (5.62)	.597
Musculoskeletal with hardware	1 (0.81)	13 (14.6)	<.001
Other	14 (11.4)	13 (14.6)	.487
Length of hospital stay, h, median (IQR)	100 (68–252)	159 (112–250)	<.001
Duration of antimicrobial use, d, median (IQR)	27.0 (21–45)	39.0 (24–95)	.011
ICU admissions, *n* (%)	18 (14.6)	32 (36.0)	<.001
Time from hospital discharge to survey, median (IQR)	13.00 (10–20)	15.0 (11–28)	.0504

IQR, interquartile range; —, not applicable.

caregivers administering oral antimicrobial therapy (2.09 of 5 vs 2.87 of 5; $P < .001$; Table 2). However, the reported comfort level with the antimicrobial treatment regimen at the time of the follow-up clinic visit did not differ between groups (Table 2). Overall, caregivers administering OPAT reported a higher burden associated with drug administration compared with the oral antimicrobial treatment group for both themselves and for their children (Table 2). A higher proportion of caregivers of children treated with OPAT reported that administering antimicrobial care was burdensome when compared with those of children who received oral therapy (Likert score ≥3; 46% vs 19%; $P < .001$). Caregivers of patients receiving oral therapy reported a higher burden of routine laboratory draws (Table 2).

Caregiver QoL

Caregivers of children treated with OPAT reported significantly lower overall QoL scores (8.8-point difference) compared with caregivers of those receiving oral antimicrobial therapy, including significant differences between groups across 7 of 8 subdomains (Fig 1). The absolute difference between groups was similar after controlling for confounders through multivariable regression (8.3 points lower for OPAT compared with oral therapy; $P < .001$). In the subgroup of subjects with diagnoses limited to osteomyelitis, complicated pneumonia, and intraabdominal infection ($n = 27$ in the OPAT group [30.3% of the total cohort]; $n = 104$ in the oral therapy group [84.5% of the total cohort]), we observed a similar difference in the QoL score between the OPAT and oral antimicrobial therapy groups (10 points lower for OPAT; $P = .01$).

Caregiver Direct and Indirect Costs

The total reported out-of-pocket expenses for caregivers using OPAT was twice that for those of patients receiving oral therapy but did not reach statistical significance (Table 3). The median number of days of missed school or day care was significantly greater for patients treated with OPAT than for patients treated with oral antimicrobial agents (13.5 vs 5.0 days; $P = .02$; Table 3). In the OPAT group, 28% of patients attended school or day care with a PICC or a catheter in place. Caregivers treating patients with OPAT reported a greater number of missed work hours compared with caregivers administering oral therapy (60.0 vs 30.0 hours; $P = .02$; Table 3). The average number of minutes per day spent administering antimicrobial agents was also greater for caregivers using OPAT compared with caregivers using oral therapy (90.0 vs 6.0 minutes; $P < .001$; Table 3). For the subgroup of patients with osteomyelitis, complicated pneumonia, and intraabdominal infection, we observed similar differences in nearly all of these measured costs. Children treated with OPAT required more time for antimicrobial administration (146.5 vs 13.1 minutes; $P < .001$) and missed more school and day care (18.1 vs 9.5 days; $P = .08$). Caregivers administering OPAT missed more work than those administering oral therapy (69.9 vs 52.6 hours; $P = .27$), but this difference was not statistically significant. The out-of-pocket expenses were similar between the OPAT and oral therapy groups ($1010 vs $1043; $P = .63$).

Direct Medical Costs of Antimicrobial Therapy

The average daily cost for OPAT administration was more than ninefold higher than that for oral therapy administration ($65 [95% confidence interval (CI): $51–$78] for OPAT compared with $7 [95% CI: $4–$9] for oral therapy, a difference of $58 [95% CI: $46–70]). For OPAT, this consisted of an average daily cost of $33 for medications, $19 for supplies and administration, and $13 for nursing visits (Fig 2). After adjustment for potential confounders by using a multivariable model, the cost of OPAT remained ninefold higher ($P < .001$), with a difference in the average daily cost of $55 (95% CI: $43–$70). In the subgroup of patients with diagnoses of osteomyelitis, complicated pneumonia, and intraabdominal infection, the adjusted average daily cost of OPAT was 11-fold higher than that of oral therapy ($P < .001$), and the difference in the average daily cost was $56 (95% CI: $36–$85).

TABLE 2 Characterization of Reported Treatment Burden for OPAT and Oral Antimicrobial Therapy

Characteristic	Oral Therapy, mean Likert score ± SD	OPAT, mean Likert score ± SD	*P*
Comfort with antimicrobial regimen at discharge	2.87 ± 1.51	2.09 ± 1.46	<.001
Comfort with antimicrobial regimen at follow-up	3.02 ± 1.59	2.82 ± 1.61	.380
Reported caregiver burden of drug administration	0.64 ± 0.84	1.30 ± 1.11	<.001
Reported patient burden of drug administration	1.04 ± 1.15	1.38 ± 1.14	.034
Reported burden of routine laboratory blood draws	1.87 ± 1.31	1.04 ± 1.17	<.001

DISCUSSION

In this study, we compared the economic burden of OPAT or oral therapy for children after hospitalization for infection. We found that the economic burden of administering OPAT, measured across multiple dimensions, including direct medical costs and indirect costs (such as days of missed work and school along with time spent administering medication) was substantially greater than for oral therapy. Additionally, we found that QoL was lower for caregivers administering OPAT compared with caregivers administering oral therapy. Collectively, these findings provide strong support for consideration of oral therapy in place of OPAT when safe, effective, and feasible alternatives exist. These data could provide inputs for future comparative-effectiveness studies for conditions in which relative risks and benefits remain uncertain between OPAT and oral therapy.

To our knowledge, this is the first economic evaluation of OPAT compared with oral therapy in children. Previous economic evaluations of pediatric OPAT have been focused on comparisons between OPAT and prolonged hospitalization.[2,20] A recent systematic review revealed that OPAT was associated with substantial cost savings compared with prolonged hospitalization across all studies analyzed, with the cost of OPAT treatment courses ranging from $1000 to >$20 000.[2] The primary economic

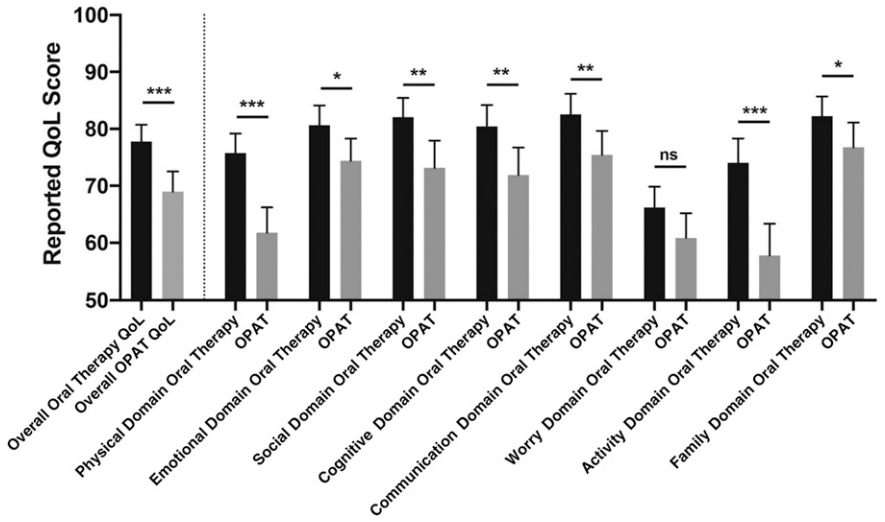

FIGURE 1 Reported caregiver QoL in the OPAT and oral antimicrobial treatment groups. Overall QoL scores and individual domain scores were significantly lower for the OPAT group compared with the group receiving oral antimicrobial agents. ns, not significant. * $P < .05$; ** $P < .01$; *** $P < .001$.

outcome in our study was the daily cost of medication administration, which was $65 for OPAT. Applied to a typical treatment episode of ~30 days in duration, the cost totals $1950, which is within the range of the studies analyzed by Bryant and Katz.[2] By using the average daily cost of oral therapy, the direct cost savings of using oral therapy across a 30-day treatment course is >$1700. This is an extremely conservative estimate of the cost difference between these 2 modes of treatment because it does not account for costs associated with OPAT, including placement of a central line and the medical costs associated with potential catheter-related complications, all of which are completely avoided with oral therapy. The avoidance of nonreimbursable time for care coordination further favors oral therapy from the health care perspective.[19]

As expected, the 2 groups of study participants were not identical at baseline. Children were more likely to be prescribed OPAT if they had central nervous system (CNS) infections or endocarditis. However, subgroup analyses restricted to patients with osteomyelitis, complicated pneumonia, or intraabdominal infections revealed similar results, with direct costs of OPAT significantly higher and caregiver QoL significantly lower when compared with those for caregivers of children receiving oral therapy. For patients with conditions that require parenteral therapy, such as endocarditis or CNS infections, our findings provide insights into the burdens associated with OPAT administration that can be used to provide appropriate anticipatory guidance for patients and their caregivers.

A growing body of evidence has revealed that for certain conditions, including complicated pneumonia and osteomyelitis, the clinical outcomes are equivalent between OPAT and oral therapy and likely favor oral therapy for most children because of lower risk of complications.[8,10,12] Our findings provide further support for the relative advantages of oral therapy in place of OPAT. For oral therapy, both the direct costs of medication administration and the indirect costs were lower, and QoL scores were higher.

We found that the burden placed on caregivers of children treated with OPAT was substantial. A strength of our study is the inclusion of indirect costs, including time spent administering therapy and QoL. Time spent administering therapy refers to "informal care," which may be substantial for children with complex health needs and may displace other important activities, including work. These measures are often not included in formal economic evaluations in pediatrics[23] and have not been included in previous evaluations of OPAT. Caregivers of children treated with OPAT reported missing 60 hours of work, compared with 30 hours for caregivers of children treated with oral therapy, over a 2-week period. Some of this difference may be attributable to the underlying illness, which differed between groups, rather than the route of treatment administration. Additionally, caregivers administering OPAT spent a median of 90 minutes per day administering treatment, compared with 6 minutes per day for caregivers administering oral antimicrobials. This amounts to 45 hours over the course of a typical 30-day treatment course dedicated to OPAT administration. We found that caregivers of patients receiving OPAT reported an overall decrease in QoL, evident across 7 of 8 subdomains (Fig 1) even after multivariable modeling. The reported decrease in QoL for caregivers administering OPAT also remained substantial in our subgroup analysis, suggesting that caregiver burden is increased regardless of clinical diagnosis.

Our study has several limitations. Although we used multivariable modeling and a subgroup analysis to adjust for differences between patients treated with OPAT and

TABLE 3 Direct and Indirect Medical Costs for OPAT and Oral Antimicrobial Therapy

Characteristic	Oral Therapy ($n = 123$)	OPAT ($n = 89$)	P
Days of missed school or day care, median (IQR)	5.00 (2.00–14.0)	13.5 (7.00–30.0)	.019
Attended school or day care with PICC and/or a catheter in place, *n* (%)	N/A	25 (28.1)	N/A
Hours caregiver missed of work, median (IQR)	30.0 (16.0–48.0)	60.0 (32.0–120)	.020
Total min per day spent administering antimicrobial agents, median (IQR)	6.00 (3.00–10.0)	90.0 (32.5–210)	<.001
Out-of-pocket expenses, $, median (IQR)	350 (145–1115)	685 (270–2910)	.212

IQR, interquartile range; N/A, not applicable.

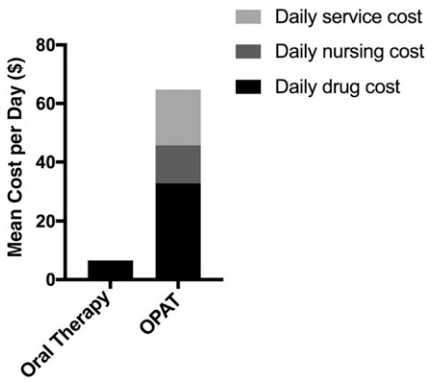

FIGURE 2 Average cost per day in US dollars of oral antimicrobial therapy and OPAT. Daily nursing costs and a daily service charge are exclusive to the OPAT group.

patients treated with oral therapy, which could impact medical costs and caregiver QoL, unmeasured confounders may still remain. In the survey, we did not collect detailed information on caregivers. Differences in education, medical experience, or social support might influence the experience with OPAT. Our survey was completed during a clinic visit a median of 14 days after discharge, and the timing was not standardized. Although our estimates for the direct medical costs of treatment administration encompassed the entire duration, additional direct and indirect medical costs for caregivers may have accrued after the survey was administered, and therefore, our estimates are conservative. Some survey questions may be subject to recall bias because caregivers were not required to keep journals or notes. Not all potentially eligible subjects were able to be approached for enrollment. This was a single-center study, and subjects were enrolled from a single infectious diseases clinic; therefore, the generalizability of our findings to other patient and caregiver populations is unknown.

This study adds to our understanding of the costs associated with OPAT for serious infections, compared with those associated with oral antimicrobial administration, and the impacts on caregivers. Our findings can be used to inform clinical decision-making by providing a strong economic rationale for clinicians to favor oral therapy in place of OPAT for treatment of conditions in which clinical outcomes are expected to be similar. The results can also be used to better inform patients and caregivers during discharge planning about the challenges associated with OPAT administration when this is the chosen therapy. The substantial economic differences between oral therapy and OPAT raise the importance of conducting cost-effectiveness analyses. Perhaps even more importantly, additional comparative-effectiveness studies between these 2 modes of therapy for conditions not traditionally treated with oral therapy are needed, including for conditions such as endocarditis and uncomplicated bloodstream infections.

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